REMARKS

Claims 1, 7, 10-27, 54-57, 59 and 60 are pending in the application. Claims 1, 7, 10-27, 54-57, 59 and 60 have been rejected. Claims 1, 7, 12, 13, 14, 15, 16, 21, 24, 54, 55, 56 and 59 have been amended. New claims 61, 62 and 63 have been added.

The amendments to the claims, specification and abstract are editorial in nature, and contain no new matter. Therefore, Applicants respectfully request entry of the Amendment.

PRIORITY

In the Office Action, the Examiner objected to the granting of the benefit of priority to the Subject Application from United States non-Provisional Application No. 09/302,457, filed on April 29, 1999. The Examiner asserted that the elected subject matter, namely the identification of a human homologue of the p-Hyde gene and its product, allegedly has priority dating back to the filing date of the instant application, alone. Applicants have requested continued examination of the subject Application, and request to elect the subject matter pertaining to the rat p-Hyde gene and its product, instead of the formerly elected human p-Hyde gene and its product.

The Examiner has stated in a previous Office Action, that the subject matter including the rat p-Hyde gene and its product may claim the benefit of United States non-Provisional Application No. 09/302,457. Accordingly, Applicants request that the Examiner withdraw the previous objection.

DRAWINGS

In the Office Action, the Examiner noted that the drawings are considered informal. In response, Applicants hereby submit an amended set of formal drawings, in compliance with PTO form 948 attached to Paper No. 27. Accordingly, Applicants request withdrawal of the rejection.

COMPLIANCE WITH THE SEQUENCE RULES

In the Office Action, the Examiner noted that statement that the content of the paper and CRF copies include no new matter as required by 37 C.F.R. 1.821 through 1.825 in insufficient since it notes that the sequence listing is "forwarded herewith" and does not refer to the sequence listing filed April 16, 2001. In response, Applicants have herein amended the sequence listing to include the translated product of SEQ ID NO: 3, which is new SEQ ID NO: 7, and hereby submit an amended statement indicating that the content of the paper and CRF copies include no new matter as required by 37 C.F.R. 1.821 through 1.825, referring to the sequence listing filed April 16, 2001, and the amended listing filed herewith. Accordingly, Applicants request withdrawal of the rejection.

OBJECTIONS TO THE SPECIFICATION

In the Office Action, the Examiner objected to the specification as allegedly containing confusing reference materials. Specifically the Examiner asserted that "[t]roughout the application, for example on page 25, line 25, bracketed reference such as "[74]" are found but do not correlate to the reference citations at the end of the application....also, "?" are found throughout the specification".

In response, Applicants have corrected the specification to deleted the "?" and to delete the reference numbers in brackets and deleted the confusing references list at the end of the specification on pages 96-101. Accordingly, Applicants respectively request that the Examiner withdraw the objection.

CLAIM REJECTIONS - 35 U.S.C. § 112 SECOND PARAGRAPH

In the Office Action, the Examiner asserted that claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the term "analogs".

In response, Applicants have amended claims 1, 7, 10-27, 54-57, and 59-60, removing all reference to the term "analog". It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Therefore Applicants respectfully request Examiner withdraws the rejection.

In response, Applicants have amended claims 1, 7, 10-27, 54-57, and 59-60, removing all reference to the term "analog". It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Therefore Applicants respectfully request acceptance of the Amendedment.

Applicants have, however, entered Claim 61, which recites fragments, analogs variants or mutants of the p-Hyde sequence. Applicants submit that the term "analogs" is defined in the Specification of the Subject Application, and is well known to the skilled person in the art. Applicants have specifically stated in the Specification in the Paragraph on Page 13, lines 22 - Page 14 line 6, that:

> "The nucleotide encoding p-Hyde includes RNA, cDNA, genomic DNA, synthetic forms, and mixed polymers, both sense and antisense strands and may be chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates, carbamates, etc.), charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), pendent moieties (e.g., polypeptides), intercalators (e.g., acridine, psoralen, etc.), chelators, alkylators, and modified linkages (e.g., alpha anomeric nucleic acids, etc.). Also included are synthetic molecules that mimic nucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule, substantially homologous to primary structural sequence but which include, e.g., in vivo or in vitro

chemical and biochemical modifications or which incorporate unusual amino acids."

Applicants further characterize the p-Hyde proteins by the nucleic acids encoding such proteins, as well as by protein sequences comprising such proteins, including any other sequences, which have 75-95% similarity/identity with disclosed sequences. Thus, Applicants have specified the metes and bounds of the term "analog", contrary to the Examiner's assertion, and Applicants respectfully request the Examiner to consider these arguments and withdraw the rejection.

In the Office Action, the Examiner rejected claim 16 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the term "sequence complementary to". In response, Applicants have herein amended claim 16 to refer to an isolated nucleic acid molecule comprising a nucleic acid sequence that is complementary to the nucleic acid sequence set forth in SEQ ID No. 3.

Both Claims 1 and 16 refer to a nucleic acid molecule. The Examiner objected to the nucleic acid molecule of claim 1 as allegedly encompassing DNA, which is double stranded and already contains a "complementary" sequence to the gene that encodes the protein. Applicants respectfully point out that as described in the specification on page 15 (lines 13-16), Applicants state that the **nucleic acid** of this invention may comprise an **RNA** or **DNA** molecule in **either single** or **double stranded form**. Applicants claims to a complementary sequence, therefore recites **complementary RNA or DNA** which may be a single stranded DNA or RNA molecule with a nucleotide sequence that is complementary to the sequence as set forth in SEQ ID NO: 3. Therefore Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

In the Office Action, the Examiner rejected claims 21-24 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention, by referring to the abbreviations "BAC".

In response, claim 21 has been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Thus Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

CLAIM REJECTIONS - 35 U.S.C. § 112 FIRST PARAGRAPH

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-56 and 59 under 35 U.S.C. § 112, first paragraph as allegedly failing to clearly define a structural limitation of the claimed nucleic acid sequences. In response, Applicants have hereby amended claims 1, 7, 10-27, 54-56 and 59 to refer to an isolated nucleic acid molecule, comprising a nucleic acid sequence encoding a rat *p-Hyde* protein, with a nucleic acid sequence as set forth in SEQ ID NO: 3. Applicants have also recited nucleic acids comprising nucleotide sequences sharing at least 75, 85 or 95 % identity with SEQ ID NO: 3, as part of the instant invention. Applicants submit that the amended claims are thus definite, and respectfully request that the Examiner withdraw the rejection.

CLAIM REJECTIONS - 35 U.S.C. § 101

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. § 101 as allegedly lacking patentable utility. Applicants respectfully traverse the Examiner's rejection. Applicants submit that the subject matter defined by the claims, namely the isolated nucleic acid molecule set forth in SEQ ID No. 3 is functionally characterized in the subject Application. Applicants have presented evidence in the Subject Application demonstrating an ability of a protein encoded by the sequences of the Subject Application to induce cell-death-susceptibility in prostate cancer cells. Further, the Examiner asserted that the rat p-Hyde protein has credible utility, and Applicants have herein amended the Application to presently elect rat p-Hyde sequences, as the human sequences will be pursued in a different Application.

Applicants therefore submit that rat p-Hyde function and thereby utility has been demonstrated in the subject Application. Therefore, the claimed isolated nucleic acid molecule has a credible patentable utility. Accordingly, Applicants respectfully request that the rejection of claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. § 101 be withdrawn.

Claims Objections

The Examiner asserted that Claim 7 is objected to for having an improper Markush group. According to the Examiner the members of a Markush group must be independent and non-overlapping. In Claim 7, the group "c-DNA" is included in the group "DNA"; thus, the Markush group is improper.

In response Applicants have amended Claim 7. Thus, claim 7 no longer contains an improper Markush group, and accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner objected to Claims 12-17 under 37 C.F.R. § 1.75 (c), as being allegedly of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim (s), or amend the claims (s) to place the claims(s) in proper depended form, or rewrite the claim(s) in independent form. According to the Examiner Claims 12-17 are drawn to complementary or antisense sequences, none of which are encompassed by Claim 1, as amended.

In response Applicants have amended Claims 12-16 and cancelled claim 17. Claim 12 is an independent claim, referring to an oligonucleotide specifically hybridizing with a nucleic acid molecule encoding a rat p-Hyde protein, wherein the nucleic acid molecule has a sequence as set forth in SEQ ID NO: 3, with claims 13-15 dependent therefrom, and claim 16 is an independent claim, referring to an isolated nucleic acid molecule having a nucleic acid sequence complementary to the sequence as set forth in SEQ ID NO: 3. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change

the literal scope of the claims in any way or result in any prosecution history estoppel. Thus, Applicants have rewritten the claims in proper independent form, and accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner asserted that Claim 14 is objected to for having allegedly an improper format and for being inconsistent with previous claims. A period is required at the end of the claim. Also, the claim should depend from Claim 14 and cite—wherein the detectable marker—and not "wherein the oligonucleotide" for consistency with previous claims.

In response Applicants have amended Claim 14. Thus amended Claim 14 has a proper format, and is now consistent with previous claims. Accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner asserted that Claim 59 is objected to for allegedly depending from a non-elected claim, Claim 53.

In response Applicants have amended Claim 59 to depend from claim 7. Thus Claim 59 properly depends from an elected claim. Accordingly, Applicants respectfully request withdrawal of the rejection.

REJECTIONS ON 35 U.S.C. § 102

In the Office Action, the Examiner rejected claims 1, 7, 12, 13, 16 and 17 under 35 U.S.C. § 102(b), as allegedly being anticipated by Hillier et al. In response, Applicants respectfully traverse this rejection in view of the remarks that follow.

Claim 1 recites an isolated nucleic acid molecule encoding for a rat p-Hyde protein having a nucleic acid sequence as set forth in SEQ ID No. 3. The Examiner has asserted that Hillier et al. disclose "a human mRNA EST sequence that matches 155 nucleotides of

Applicants' SEQ ID No: 1". Applicants maintain that Hillier et al do not anticipate the instant invention.

The nucleotide sequence disclosed by Hillier et al., is not a p-Hyde coding sequence as set forth in SEQ ID No. 3. In order for Hillier et al to be anticipatory of claim 12, the Hillier nucleotide sequence must disclose the p-Hyde coding sequence. Hillier et al., do not disclose oligonucleotides per se, and do not disclose a sequence encoding p-Hyde, as the sequence disclosed by Hillier et al does not in fact code for a functional protein. Thus Applicants submit that Hillier et al., does not anticipate claims 1 or 12.

Claim 16 has been amended to recite an isolated nucleic acid molecule comprising a nucleic acid sequence complementary to that set forth in SEQ ID No. 3. As in claim 1, Hillier et al do not disclose the full p-Hyde coding sequence, and hence does not anticipate claim 16. Applicants respectfully assert that amended independent claims 1, and dependent claim 7, 12 and dependent claim 13, and 16, are allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections to claims 1, 7, 12, 13 and 16.

Further, in the Office Action, the Examiner rejected claims 1, 7, 10-21, 25-27, 54-56 and 59 under 35 U.S.C. § 102(b), as being anticipated by Talerman et al. In response, Applicants respectfully traverse this rejection in view of the remarks that follow.

The Examiner asserted that Talerman et al. disclose "a DNA sequence that is 72% similar and 39% identical to Applicants' SEQ ID No: 1". Claim 1 recites an isolated nucleic acid molecule encoding for a rat p-Hyde protein having a nucleic acid sequence as set forth in SEQ ID No. 3. SEQ ID NO: 3 comprises a 1467 nucleotide sequence encoding for rat p-Hyde. Alignment of the TSAP 6 sequence recited in Talerman, shows that TSAP 6 shares less than 50 % identity with the entire nucleotide sequence of SEQ ID NO: 3. Thus, the p-Hyde encoding nucleic acids of this invention differ structurally and functionally from TSAP 6, as disclosed in Talerman et al.

Further, the nucleotide sequence disclosed by Talerman et al., does not encode for a functionally comparable protein. Talerman et al discloses TSAP sequences, which are known to function in upregulation of apoptosis in a p53-dependent manner, following p53 induction. In the instant invention, however, p-Hyde functions through a different mechanism, acting as both a tumor suppressor, and as an apoptotic inducer, via its ability to impair DNA repair enzyme function. Talerman et al do not disclose a molecule that functions to impair DNA repair enzyme function. Thus TSAP as disclosed by Talerman et al., differs from the instant invention, and therefore does not anticipate Claim 1, or dependent claims thereof. Claims 7, 10, 11, 18-21, 25-27 and 59 directly depend from claim 1, and therefore Applicants maintain is not anticipated by Tallerman et al., accordingly.

Claim 12 has been amended to recite an oligonucleotide of at least 15 bases capable of specifically hybridizing with a nucleic acid molecule encoding a mammalian p-Hyde protein having a sequence as set forth in SEQ ID No. 3. In order for Talerman et al to be anticipatory of claim 12, the nucleotide sequence disclosed by Talerman et al. must teach the nucleotide sequences from which an oligonucleotide specifically hybridizing with a nucleic acid sequence encoding for p-Hyde protein are designed. Talerman et al., do not teach a sequence encoding p-Hyde, thus Applicants submit that Talerman et al., does not anticipate claim 12. Claims 13-15 directly depend from claim 12, and therefore Applicants maintain is not anticipated by Talerman, et al., accordingly.

Claim 16 has been amended to recite an isolated nucleic acid molecule comprising a nucleic acid sequence complementary to that set forth in SEQ ID No. 3. As in claim 1, Talerman et al., do not disclose a sequence encoding p-Hyde, and hence do not anticipate claim 16. Accordingly, Applicants respectfully assert that amended independent claim 16 is allowable.

As discussed above, the Talerman TSAP 6 sequence shares less than 50% identity with rat p-Hyde as disclosed in SEQ ID NO: 3, and differs functionally as well. Applicants

claims refer to isolated nucleic acids with a nucleotide sequence sharing at least 75, 85 or 95% identity with SEQ ID NO: 3, and therefore Applicants maintain that claims 54-56 are not anticipated by Talerman et al, as the p-Hyde sequences of the instant invention significantly differ, both structurally and functionally, from that of TSAP 6. Accordingly, Applicants request withdrawal of the rejection.

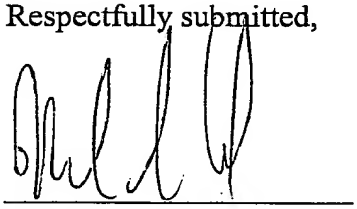
Therefore, Applicants respectfully assert that claims 1, 7, 10-21, 25-27, 54-56 and 59 are allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the objections to the claims.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 05-0649.

Respectfully submitted,



Mark S. Cohen
Attorney for Applicant(s)
Registration No. 42,425

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Eitan, Pearl, Latzer & Cohen Zedek, LLP
10 Rockefeller Plaza, Suite 1001
New York, NY 10020
Telephone: (212) 632-3494
Fax: (212) 632-3489